Keratocyte Fragments and Cells Utilize Competing Pathways to Move in Opposite Directions in an Electric Field.

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Public Summary:
In order to better guide migration of stem cells, we also seek to understand the molecular and cellular mechanisms that the cells respond to electrical signals. In this publication, we used a very unique model system - cell fragments. This is a part of the cells without nuclear, and major organelles. it is a minimal unit know to migrate. Using this system, we showed that the mechanisms of sensing and decision on which direction to migrate in are separate. Motor machinery - acto-myosin and actin plays tug-of-war and determine which direction to migrate. it is possible to regulate this motor machinery to regulate directional response of cells.

Scientific Abstract:
Sensing of an electric field (EF) by cells-galvanotaxis-is important in wound healing [1], development [2], cell division, nerve growth, and angiogenesis [3]. Different cell types migrate in opposite directions in EFs [4], and the same cell can switch the directionality depending on conditions [5]. A tug-of-war mechanism between multiple signaling pathways [6] can direct Dictyostelium cells to either cathode or anode. Mechanics of motility is simplest in fish keratocytes, so we turned to keratocytes to investigate their migration in EFs. Keratocytes sense electric fields and migrate to the cathode [7, 8]. Keratocyte fragments [9, 10] are the simplest motile units. Cell fragments from leukocytes are able to respond to chemotactic signals [11], but whether cell fragments are galvanotactic was unknown. We found that keratocyte fragments are the smallest motile electric field-sensing unit: they migrate to the anode, in the opposite direction of whole cells. Myosin II was essential for the direction sensing of fragments but not for parental cells, while PI3 kinase was essential for the direction sensing of whole cells but not for fragments. Thus, two signal transduction pathways, one depending on PI3K, another on myosin, compete to orient motile cells in the electric field. Galvanotaxis is not due to EF force and does not depend on cell or fragment size. We propose a "compass" model according to which protrusive and contractile actomyosin networks self-polarize to the front and rear of the motile cell, respectively, and the electric signal orients both networks toward cathode with different strengths.